

Metal Based Ethanolamine Derived Compounds: A note on their Synthesis, Characterization and Bioactivity

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Abstract

Metal-based ethanolamines, (L¹)-(L⁴) coordinated with Co(II), Cu(II), Ni(II) and Zn(II) metals in 1:2 (metal:ligand) molar ratio to produce new compounds have been reported. These compounds were screened for their bactericidal/fungicidal activity against a number of bacterial (*Escherichia coli*, *Shigella flexneri*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Staphylococcus aureus* and *Bacillus subtilis*) and fungal strains (*Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glabrata*) alongside against a shrimp species known as *Artemia salina*. The screening results indicated that metal complexes have significantly higher activity than uncomplexed ligands against one or more bacterial/fungal species due to chelation. The ligand (L⁴) displayed good bacterial and fungal activity as compared to other ligands. The antibacterial results revealed that the Zn(II) complex (16) of (L⁴) was found to be the most active complex and Co(II) complex (14) of the same ligand (L⁴), demonstrated the highest antifungal activity.

Keywords: Ethanolamine derived compounds, Metal(II) complexes, Antibacterial/antifungal

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Introduction

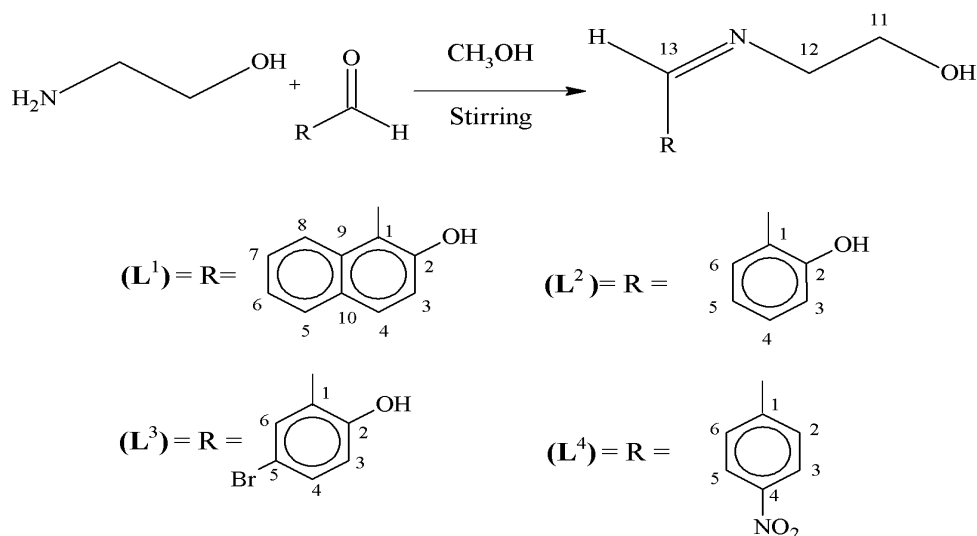
Bio-active transition metal complexes have gained increasing interest in metal based drug chemistry especially as therapeutic agents. Since their discovery in 1864, Schiff bases have contributed immensely to the development of co-ordination chemistry and acting as an inspiration for the development of novel compounds¹. Schiff bases are characterised by an imine group and are formed as a condensation product² of primary amine with an aldehyde or ketone in the presence of a dehydrating agent such as MgSO₄. A number of Schiff base metal complexes have displayed bioactivity as antibacterial^{3,4} antifungal⁵, anticancer^{6,7A-B}, anti-inflammatory⁸, anticonvulsant⁹, antiviral¹⁰ and analgesic¹¹ agents. Although metal based ethanolamines have historically been subject of many investigations^{12,13} due to their use as buffers¹⁴, catalysts¹⁵, inhibitors¹⁶, ion exchangers¹⁷, electroplating and dyes¹⁸, now they are garnering attention for their biological¹⁹ role in plant growth²⁰ regulation, bacterial and fungal metabolism and as a cytotoxic agent²¹. Metal based compounds have also been reported to improve electron transfer and efficiency in protein bioelectrochemistry^{22a,b}.

One of the advantages of using Schiff bases is the ability to control and tune the electronic and steric properties of the ligand attached to the metal. One of the strategies is an appropriate choice of precursor, because that plays a pivotal role by allowing control over nature of donor atoms, number of chelating moieties and the extent of denticity. The new series of ethanolamine derived compounds **(L¹)-(L⁴)**, *(E)*-2-(((2-hydroxyethyl)imino)methyl)phenol (**L¹**), *(E)*-2-(((2-hydroxyethyl)imino)methyl)naphthalen-1-ol (**L²**), *(E)*-2-(((4-nitrobenzylidene)amino)ethanol (**L³**) and *(E)*-5-bromo-2-(((2-hydroxyethyl) imino)methyl)phenol (**L⁴**) were synthesized from the reaction of 2-hydroxy-1-naphthaldehyde, 2-hydroxybenzaldehyde, 5-bromo-2-hydroxybenzaldehyde and 4-nitrobenzaldehyde respectively, with ethanolamine in equimolar ratio (Scheme 1). The synthesized ligands were further coordinated with Co(II), Cu(II), Ni(II) and Zn(II) metals in 1:2 (metal:ligand) molar ratio to produce new metal complexes (Scheme 2). The synthesized ligands and their metal(II) complexes have been screened *in vitro* for anti-bacterial activity against six bacterial species (*Escherichia coli*, *Shigella flexneri*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Staphylococcus aureus* and *Bacillus subtilis*) and for *in vitro* anti-fungal activity against six fungal strains (*Trichophyton longifusus*, *Candida albicans*, *Aspergillus*

flavus, *Microsporum canis*, *Fusarium solani* and *Candida glabrata*). Cytotoxicity of the compounds was determined through the help of brine shrimp bioassay.

Materials and Methods

All the chemicals used were of analytical grade and were purchased from Sigma Aldrich. Infrared spectra of solid compounds (as KBr disc) were recorded on a Nicolet FT-IR Impact 400D infrared spectrometer. Elemental analysis was carried out on Perkin Elmer and ^1H and ^{13}C NMR spectra were recorded on a Bruker Spectrospin Avance DPX-400 spectrometer using TMS as internal standard and d_6 -DMSO as a solvent. Electron impact mass spectra (EIMS) were recorded on JEOL MSRoute instrument. UV-Visible spectra were recorded on ultraviolet spectrometer-1700 (Shimadzu, Japan) in the frequency range of 250-800 nm. Molar conductance of metal complexes was measured using an Inolab Cond 720 Conductivity Bridge at room temperature using 0.001 molar solutions in DMF. A Stanton SM12/S Gouy balance was used to measure the magnetic susceptibility of the metal complexes at room temperature using mercury acetate ligand as a standard. *In vitro* antibacterial, antifungal and cytotoxic properties were studied in collaboration with Research Institute of Chemistry, International Centre for Chemical Sciences, University of Karachi, Pakistan and School of Science and Engineering, Teesside University, UK.



(Scheme 1) Preparation of Ligands

Synthesis of Ligands

Different aldehydes such as 2-hydroxy-1-naphthaldehyde, 2-hydroxybenzaldehyde, 5-bromo-2-hydroxybenzaldehyde and 4-nitrobenzaldehyde were individually dissolved in ethanol (25 mL) and added respectively to a refluxed solution of ethanolamine in ethanol (10 mL) in an equimolar ratio. The reaction mixture was refluxed for 3 hours and consequently precipitated while being monitored. The solid product thus obtained was filtered, washed with ethanol and dried. It was re-crystallized in hot ethanol/methanol (1:1). The same method was used for the preparation of all other ligands (**L**¹)-(**L**⁴).

(E)-2-(((2-Hydroxyethyl)imino)methyl)naphthalen-1-ol (L¹)

Yield: (1.64 g, 76%); mp 151°C; color (dark yellow); IR (KBr, cm⁻¹): 3438 (aryl-OH), 3385 (alc-OH), 1627 (-HC=N), 1603 (C-H) and 1584 (C=C); ¹H NMR (ppm d₆-DMSO): δ 3.65 (s, 1H, alc-OH), 4.50 (t, 2H, C₁₂-H), 5.85 (t, 2H, C₁₁-H), 7.15 (d, 1H, *J* = 9.0 Hz, C₃-H), 7.41 (t, 1H, *J* = 7.4 Hz, C₆-H), 7.53 (t, 1H, *J* = 7.4 Hz, C₇-H), 7.80 (d, 1H, *J* = 7.8 Hz, C₄-H), 7.95 (d, 1H, *J* = 9.0 Hz, C₅-H), 8.22 (d, 1H, *J* = 8.5 Hz, C₈-H), 8.53 (s, 1H, C₁₃-H), 9.88 (s, 1H, aryl-OH); ¹³C NMR (DMSO-d₆): δ 59.3 (C₁₁), 69.5 (C₁₂), 116.4 (C₁), 122.1 (C₆), 125.5 (C₃), 126.2 (C₈), 126.9 (C₁₀), 127.7 (C₇), 128.9 (C₅), 134.3 (C₉), 136.4 (C₄), 159.6 (C₂), 162.8 (C₁₃); Mass Spectrum (ESI): [M]⁺ = 215.25. Anal. Calc. for C₁₃H₁₃NO₂ (215.25) C, 72.54; H, 6.09; N, 6.51; O, 14.87 and found C, 72.48; H 6.04; O, 14.83

(E)-2-(((2-Hydroxyethyl)imino)methyl)phenol²⁰ (L²)

Yield (1.22 g, 74%); mp 92°C; color (yellow); IR (KBr, cm⁻¹): 3450 (aryl-OH), 3380 (alc-OH), 1625 (-HC=N) and 1596 (C=C); ¹H NMR (ppm d₆-DMSO): δ 3.63 (s, 1H, alc-OH), 4.50 (t, 2H, C₁₂-H), 5.85 (t, 2H, C₁₁-H), 7.0 (t, 1H, *J* = 8.5 Hz, C₄-H), 7.11 (d, 1H, *J* = 7.9 Hz, C₆-H), 7.45 (t, 1H, *J* = 7.5 Hz, C₅-H), 7.69 (d, 1H, *J* = 7.8 Hz, C₃-H), 8.50 (s, 1H, C₁₃-H), 9.91 (s, 1H, aryl-OH); ¹³C NMR (DMSO-d₆): δ 59.4 (C₁₁), 69.7 (C₁₂), 117.5 (C₃), 119.3 (C₁), 121.7 (C₅), 131.1 (C₆), 133.6 (C₄), 159.9 (C₂), 162.5 (C₁₃); Mass Spectrum (ESI): [M]⁺ = 165.19. Anal. calcd. for C₉H₁₁NO₂ (165.19): C, 65.44; H, 6.71; N, 8.48; O, 19.37. Found: C, 65.38; H, 6.67; N, 19.33.

(E)-4-Bromo-2-(((2-hydroxyethyl)imino)methyl)phenol (L³)

Yield (1.51 g, 78%); mp: 99°C, color (orange yellow); IR (KBr, cm^{-1}): 3453 (aryl-OH), 3382 (alc-OH), 1622 ($-\text{HC}=\text{N}$) and 1590 ($\text{C}=\text{C}$); ^1H NMR (ppm d_6 -DMSO): δ 3.67 (s, 1H, alc-OH), 4.50 (t, 2H, C_{12} -H), 5.85 (t, 2H, C_{11} -H), 7.12 (d, 1H, $J = 8.7$ Hz, C_3 -H), 7.50 (dd, 1H, $J = 8.7$, 2.5 Hz, C_5 -H), 8.10 (d, 1H, $J = 2.5$ Hz, C_6 -H), 8.57 (s, 1H, C_{13} -H), 9.93 (s, 1H, aryl-OH); ^{13}C NMR (DMSO- d_6): δ 58.9 (C_{11}), 68.1 (C_{12}), 118.7 (C_3), 122.5 (C_1), 125.2 (C_5), 127.7 (C_4), 133.1 (C_6), 159.2 (C_2), 161.9 (C_{13}); Mass Spectrum (ESI): $[\text{M}]^+ = 165.19$. Anal. calcd. for $\text{C}_9\text{H}_{10}\text{BrNO}_2$ (244.1): C, 44.29; H, 4.13; Br, 32.74; N, 5.74. Found: C, 44.23; H, 4.11; Br, 32.68; N, 5.70.

(E)-2-((4-Nitrobenzylidene)amino)ethanol (L^4)

Yield (1.55 g, 80%); mp: 88°C, color (reddish brown); IR (KBr, cm^{-1}): 3460 (aryl-OH), 3390 (alc-OH), 1632 ($-\text{HC}=\text{N}$), 1595 ($\text{C}=\text{C}$) and 1424 (NO_2); ^1H NMR (ppm d_6 -DMSO): δ 3.69 (s, 1H, alc-OH), 4.50 (t, 2H, C_{12} -H), 5.85 (t, 2H, C_{11} -H), 8.10 (dd, 2H, $J = 8.7$, 2.5 Hz, C_2 -H and C_6 -H), 8.33 (dd, 2H, $J = 8.7$, 2.5 Hz, C_3 -H and C_5 -H), 8.65 (s, 1H, C_{13} -H); ^{13}C NMR (DMSO- d_6): δ 59.3 (C_{11}), 68.6 (C_{12}), 120.6 (C_3), 122.4 (C_5), 130.5 (C_1), 131.0 (C_6), 152.3 (C_4), 158.8 (C_2), 162.2 (C_{13}); Mass Spectrum (ESI): $[\text{M}]^+ = 194.19$. Anal. calcd. for $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_3$ (194.19): C, 55.67; H, 5.19; N, 14.44. Found: C, 55.62; H, 5.16; N, 14.11.

Synthesis of the Transition Metal(II) Complexes

All complexes were prepared according to the standard procedure in which a methanol solution (20 mL) of the respective metal(II) as a chloride (5 mmol) was added to a refluxed methanol solution (30 mL) of the ligand (10 mmol). The mixture was further refluxed for 3 h leading to a precipitated product. It was then cooled to room temperature, filtered, washed with methanol and finally with diethyl ether. The precipitated product thus obtained was dried and recrystallized in a mixture of hot aqueous methanol:ethanol (1:2) to obtain TLC pure product.

NMR data of the Zn(II) complexes

$[\text{Zn}(\text{L}^1)_2]$ (4): ^1H NMR (DMSO- d_6 , δ , ppm): 3.78 (s, 1H, alc-OH), 4.61 (t, 2H, C_{12} -H), 5.91 (t, 2H, C_{11} -H), 7.26 (d, 1H, C_3 -H), 7.46 (t, 1H, C_6 -H), 7.59 (t, 1H, C_7 -H), 7.90 (d, 1H, C_4 -H), 7.99 (d, 1H, C_5 -H), 8.26 (d, 1H, C_8 -H), 8.64 (s, 1H, C_{13} -H); ^{13}C NMR (DMSO- d_6 , δ , ppm): 60.1 (C_{11}),

70.3 (C₁₂), 117.5 (C₁), 129.1 (C₆), 125.5 (C₃), 126.7 (C₈), 127.5 (C₁₀), 128.2 (C₇), 129.6 (C₅), 135.0 (C₉), 136.4 (C₄), 160.6 (C₂), 163.9 (C₁₃).

[Zn(L²)₂] (8): ¹H NMR (DMSO-d₆, δ, ppm): 3.79 (s, 1H, alc-OH), 4.62 (t, 2H, C₁₂-H), 5.94 (t, 2H, C₁₁-H), 7.07 (t, 1H, C₄-H), 7.18 (d, 1H, C₆-H), 7.51 (t, 1H, C₅-H), 7.79 (d, 1H, C₃-H), 8.63 (s, 1H, C₁₃-H); ¹³C NMR (DMSO-d₆, δ, ppm): δ 60.4 (C₁₁), 70.7 (C₁₂), 117.5 (C₃), 119.3 (C₁), 123.3 (C₅), 131.1 (C₆), 134.2 (C₄), 161.0 (C₂), 163.6 (C₁₃).

[Zn(L³)₂] (12): ¹H NMR (DMSO-d₆, δ, ppm): 3.70 (s, 1H, alc-OH), 4.60 (t, 2H, C₁₂-H), 5.95 (t, 2H, C₁₁-H), 7.23 (d, 1H, C₃-H), 7.55 (dd, 1H, C₅-H), 8.19 (d, 1H, C₆-H), 8.61 (s, 1H, C₁₃-H); ¹³C NMR (DMSO-d₆, δ, ppm): δ 59.8 (C₁₁), 69.1 (C₁₂), 118.7 (C₃), 123.5 (C₁), 125.7 (C₅), 128.3 (C₄), 133.8 (C₆), 160.2 (C₂), 163.0 (C₁₃).

[Zn(L⁴)₂] (16): ¹H NMR (DMSO-d₆, δ, ppm): 4.59 (t, 2H, C₁₂-H), 5.93 (t, 2H, C₁₁-H), 8.18 (dd, 2H, C₂-H and C₆-H), 8.39 (dd, 2H, C₃-H and C₅-H), 8.62 (s, 1H, C₁₃-H), 10.3 (s, 4H, H₂O); ¹³C NMR (DMSO-d₆, δ, ppm): δ 60.2 (C₁₁), 69.7 (C₁₂), 121.4 (C₃), 122.9 (C₅), 131.5 (C₁), 131.8 (C₆), 152.9 (C₄), 159.7 (C₂), 163.3 (C₁₃).

Biological Activity

Antibacterial Activity (*in vitro*)

All the newly synthesized ethanolamine derived compounds (**L¹**)-(**L⁴**) and their metal(II) complexes (**1**)-(**16**) were screened *in-vitro* for their antibacterial activity against four Gram-negative (*E. coli*, *S. flexneri*, *P. aeruginosa*, *S. typhi*) and two Gram-positive (*S. aureus*, *B. subtilis*) bacterial strains by agar-well diffusion method²⁴. The wells (6 mm in diameter) were dug in the media with the help of a sterile metallic borer with centers at least 24 mm apart. Two to eight hours old bacterial inocula containing approximately 10⁴-10⁶ colony-forming units (CFU/mL) were spread on the surface of the nutrient agar with the help of a sterile cotton swab. The recommended concentration of the test sample (1mg/mL in DMSO) was introduced in the respective wells. Other wells supplemented with DMSO and reference antibacterial drug (imipenem) served as a negative and positive control, respectively. The plates were incubated at 37°C for 24 h. Activity was determined by measuring the diameter of clear zones showing

complete inhibition (mm). In order to confirm the effect of DMSO in the biological screening, alternate studies on DMSO solution showed no activity against any bacterial strains.

Antifungal Activity (*in vitro*)

Antifungal activity was studied against six fungal strains (*T. longifusus*, *C. albican*, *A. flavus*, *M. canis*, *F. solani* and *C. glabrata*). Sabouraud dextrose agar (Oxoid, Hampshire, England) was seeded with 10^5 (cfu) mL^{-1} fungal spore suspensions and transferred to petri plates. Discs soaked in 20 mL (200 $\mu\text{g/mL}$ in DMSO) of the compounds were placed at different positions on the agar surface. The plates were incubated at 32°C for 7 days. The results were recorded as %age of inhibition and compared with standard drugs miconazole and amphotericin B.

Minimum Inhibitory Concentration (MIC)

Compounds containing promising antibacterial activity were selected for minimum inhibitory concentration (MIC) studies. The minimum inhibitory concentration was determined using the disc diffusion technique²⁵ by preparing discs containing diluted samples at 10, 25, 50 and 100 $\mu\text{g mL}^{-1}$ concentrations of the compounds along with standards at the same concentrations.

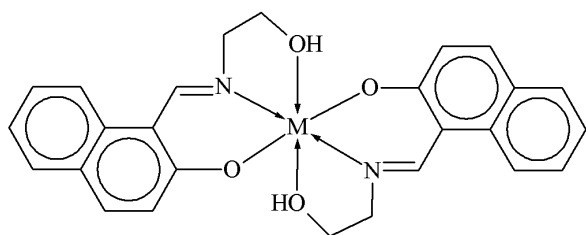
Cytotoxicity (*In vitro*)

Brine shrimp assay was done using the protocol of Meyer et al.²⁶, the details of which are reproduced here. Brine shrimp (*Artemia salina* leach) eggs were hatched in a shallow rectangular plastic dish (22×32 cm), filled with artificial seawater prepared from commercial salt mixture and double distilled water. An unequal partition was made in the plastic dish with the help of a perforated device where approximately 50 mg of eggs were sprinkled into the darkened larger compartment while smaller matter compartment was exposed to the ordinary light. After two days, nauplii were collected from the unsheltered side. A sample of the test compound was prepared by dissolving 20 mg of each compound in 2 mL of DMF. From this stock solutions 5, 50 and 500 $\mu\text{g/mL}$ were transferred to 9 vials (three for each dilutions were used for each test sample and LD_{50} was calculated as the mean of these three values) and one vial was kept as control having 2 mL of DMF only. The solvent was allowed to evaporate overnight. After two days, when shrimp larvae were ready, 1 mL of seawater and 10 shrimps were added to each vial

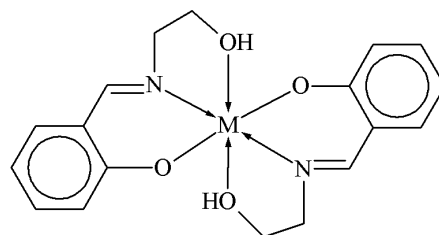
(30 shrimps/ dilution) and the volume was adjusted with seawater to 5 mL per vial²⁶. After 24 h the number of survivors was counted. Data were analyzed by a computer program to determine the LD₅₀ values²⁷.

Results and Discussion

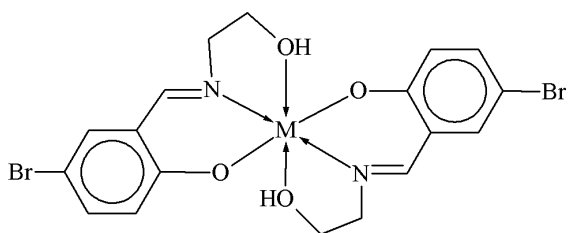
The condensation reaction of ethanolamine with 2-hydroxy-1-naphthaldehyde/2-hydroxybenzaldehyde/5-bromo-2-hydroxybenzaldehyde/4-nitrobenzaldehyde in an equimolar ratio afforded four ligands (**L**¹)-(**L**⁴) (**Scheme 1**). These coloured ligands were stable in both air and moisture. These microcrystalline solids melted at 155-280 °C and were soluble in DMSO and DMF at room temperature and in methanol and ethanol on heating. The ligands (**L**¹)-(**L**³) were found to be tridentate and (**L**⁴) to be bidentate which reacted readily with Co(II), Cu(II), Ni(II) and Zn(II) metals as their chlorides in methanol to form their metal(II) complexes (**Scheme 2**).



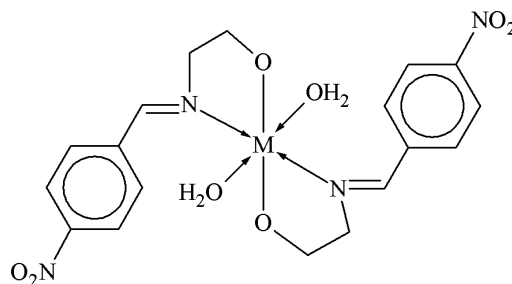
Metal(II) Complexes (1)-(4) with (L**¹)**



Metal(II) Complexes (5)-(8) with (L**²)**



Metal(II) Complexes (9)-(12) with (L**³)**



Metal(II) Complexes (13)-(16) with (L**⁴)**

(Scheme 2): Co(II), Cu(II), Ni(II) and Zn(II) Metal Complexes (1)-(16) with (L**¹)-(**L**⁴)**

(Scheme 2) Metal(II) Complexes

All the synthesized metal(II) complexes were microcrystalline and had an intense color except Zn(II) complexes which were off-white. The metal(II) complexes decomposed without melting and were insoluble in common organic solvents such as ethanol, methanol, dichloromethane and acetone but soluble in DMSO and DMF. The spectral data and elemental analysis of the prepared ligands and their metal(II) complexes were in a good agreement with their proposed structures, indicating the high purity of all the compounds. The analytical data of the complexes indicated a 1:2 metal: ligand stoichiometry.

Table 1. Physical Measurements and Analytical Data of Metal(II) Complexes (1)-(16).

No	Structure	Yield (%)	MW/ Formula	M.P (°C)	Elemental Analysis (%)			
					Calc (Found)			
					C	H	N	M
(1)	[Co(L ¹ -H) ₂]	70	[487.41] C ₂₆ H ₂₄ N ₂ O ₄ Co	166-168	64.07 (64.01)	4.96 (4.92)	5.75 (5.72)	12.09 (12.04)
(2)	[Ni(L ¹ -H) ₂]	70	[487.17] C ₂₆ H ₂₄ N ₂ O ₄ Ni	220-222	64.10 (64.01)	4.97 (4.92)	5.75 (5.71)	12.05 (12.01)
(3)	[Cu(L ¹ -H) ₂]	75	[492.02] C ₂₆ H ₂₄ N ₂ O ₄ Cu	185-187	64.77 (64.71)	4.92 (4.89)	5.69 (5.65)	12.92 (12.88)
(4)	[Zn(L ¹ -H) ₂]	83	[493.89] C ₂₆ H ₂₄ N ₂ O ₄ Zn	197-199	63.23 (63.18)	4.90 (4.86)	5.67 (5.62)	13.24 (13.20)
(5)	[Co(L ² -H) ₂]	71	[387.30] C ₁₈ H ₂₀ N ₂ O ₄ Co	175-176	55.82 (55.77)	5.21 (5.18)	7.23 (7.20)	15.22 (15.18)
(6)	[Ni(L ² -H) ₂]	74	[387.06] C ₁₈ H ₂₀ N ₂ O ₄ Ni	230-232	55.86 (55.80)	5.21 (5.17)	7.24 (7.20)	15.16 (15.12)
(7)	[Cu(L ² -H) ₂]	81	[391.91] C ₁₈ H ₂₀ N ₂ O ₄ Cu	194-196	55.16 (55.11)	5.14 (5.10)	7.15 (7.12)	16.21 (16.17)
(8)	[Zn(L ² -H) ₂]	82	[393.77] C ₁₈ H ₂₀ N ₂ O ₄ Zn	270-272	54.90 (54.85)	5.12 (5.09)	7.11 (7.06)	16.61 (16.56)
(9)	[Co(L ³ -H) ₂]	85	[545.09] C ₁₈ H ₁₈ Br ₂ N ₂ O ₄ Co	225-227	39.66 (39.61)	3.33 (3.29)	5.14 (5.11)	10.81 (10.77)
(10)	[Ni(L ³ -H) ₂]	80	[544.85] C ₁₈ H ₁₈ Br ₂ N ₂ O ₄ Ni	194-196	39.68 (39.64)	3.33 (3.29)	5.14 (5.10)	10.77 (10.73)
(11)	[Cu(L ³ -H) ₂]	84	[549.70] C ₁₈ H ₁₈ Br ₂ N ₂ O ₄ Cu	214-216	39.33 (39.29)	3.30 (3.27)	5.10 (5.07)	11.56 (11.52)
(12)	[Zn(L ³ -H) ₂]	80	[551.56] C ₁₈ H ₁₈ Br ₂ N ₂ O ₄ Zn	211-212	39.20 (39.15)	3.29 (3.26)	5.08 (5.04)	11.86 (11.82)

(13)	[Co(L ³ -H) ₂]	74	[481.32] C ₁₈ H ₂₂ N ₄ O ₈ Co	176-177	44.92 (44.87)	4.61 (4.57)	11.64 (11.60)	12.24 (12.20)
(14)	[Ni(L ³ -H) ₂]	82	[481.07] C ₁₈ H ₂₂ N ₄ O ₈ Ni	206-208	44.94 (44.89)	4.61 (4.58)	11.65 (11.60)	12.20 (12.16)
(15)	[Cu(L ³ -H) ₂]	77	[485.84] C ₁₈ H ₂₂ N ₄ O ₈ Cu	190-191	44.49 (44.44)	4.56 (4.53)	11.53 (11.50)	13.08 (13.05)
(16)	[Zn(L ³ -H) ₂]	78	[487.80] C ₁₈ H ₂₂ N ₄ O ₈ Zn	278-280	44.32 (44.27)	4.55 (4.51)	11.49 (11.45)	13.41 (13.37)

IR Spectra

The significant and distinctive IR spectral bands are reported in the experimental part and in **Table 2**. All Schiff base ligands possessed potentially active donor sites capable of coordinating with metal atoms such as azomethine nitrogen (-HC=N), aliphatic and aromatic hydroxyl (-OH) groups. The Schiff bases (**L**¹)-(**L**⁴) possessed the characteristic azomethine (-HC=N) stretching²⁸ at 1622-1632 cm⁻¹ giving a clue of condensation product. All the ligands (**L**¹)-(**L**⁴) displayed aliphatic hydroxyl (-OH) stretching at 3380-3390 cm⁻¹, however, ligands (**L**¹)-(**L**³) additionally showed aromatic hydroxyl (-OH) stretching²⁹ at 3438-3390 cm⁻¹. The ligand (**L**⁴) showed a band at 1424 cm⁻¹ resulting from NO₂ vibrations. The comparison of the IR spectra of the Schiff bases (**L**¹)-(**L**⁴) with their metal(II) complexes (**1**)-(**16**) indicated that the Schiff bases were principally coordinated to the metal(II) atoms in a bi- and tridentate fashion. The vibrations of azomethine-N group present in all the metal complexes (**1**)-(**16**) and aliphatic-O appearing in the spectra of metal(II) complexes (**1**)-(**12**) shifted to lower frequency (07-15 cm⁻¹) at 1608-1623 and 3365-3377 cm⁻¹ respectively, representing the mode of coordination of the azomethine nitrogen³⁰ and hydroxyl-O with the metal(II) atoms. Absence of bands at 3438-3490 and 3380-3390cm⁻¹ due to aliphatic and aromatic ν(OH) and consequent appearance of a new band³¹ at 1370-1377 cm⁻¹ attributed to ν(C-O) in the metal(II) complexes (**1**)-(**16**), confirmed the deprotonation and coordination of aromatic and aliphatic ν(OH) to the metal(II) atoms. The following observations further support the mode of chelation:

- Appearance of the new bands at 520-543 and 440-460 cm⁻¹ could be assigned to ν(M-O) and ν(M-N) vibrations³² in the metal complexes which are absent in ligands.

- The metal(II) complexes **(13)-(16)** demonstrated³³ new broad bands at 3468-3478 cm⁻¹ which can likely be attributed to water molecules coordinated to the metal atoms. These bands were only observed in the spectra of the metal complexes.

These clues supported the evidence of the participation of azomethine-N and deprotonation/coordination of hydroxyl-O with the metal(II) ions.

Table 2. Conductivity, Magnetic and Spectral Data of Metal(II) Complexes (1)-(16)

No	Ω_M ($\Omega^{-1}\text{cm}^2\text{mol}^{-1}$)	B.M μ_{eff}	λ_m (cm^{-1})	IR (cm^{-1})
(1)	15.9	4.35	8723, 17690, 29820	3370 (OH), 1616 (HC=N), 1370 (C-O), 520 (M-N), 442 (M-O)
(2)	15.7	3.56	8635, 17717, 25817, 29781	3372 (OH), 1615 (HC=N), 1372 (C-O), 535 (M-N), 450 (M-O)
(3)	14.6	1.66	8897, 17783, 29816	3371 (OH), 1620 (HC=N), 1373 (C-O), 529 (M-N), 448 (M-O)
(4)	14.9	Dia	28915	3373 (OH), 1618 (HC=N), 1371 (C-O), 533 (M-N), 450 (M-O)
(5)	16.2	4.53	8650, 17729, 29841	3366 (OH), 1612 (HC=N), 1372 (C-O), 522 (M-N), 446 (M-O)
(6)	15.8	3.41	8712, 17761, 25778, 29738	3365 (OH), 1610 (HC=N), 1370 (C-O), 536 (M-N), 445 (M-O)
(7)	15.6	1.71	8937, 17892, 29812	3365 (OH), 1615 (HC=N), 1371 (C-O), 526 (M-N), 443 (M-O)
(8)	15.1	Dia	28928	3368 (OH), 1613 (HC=N), 1373 (C-O), 532 (M-N), 440 (M-O)
(9)	16.2	4.38	8680, 17523, 29831	3368 (OH), 1611 (HC=N), 1377 (C-O), 540 (M-N), 449 (M-O)
(10)	15.2	3.48	8786, 17777, 25719, 29781	3367 (OH), 1610 (HC=N), 1376 (C-O), 524 (M-N), 453 (M-O)
(11)	16.0	1.74	8727, 17765, 29788	3370 (OH), 1612 (HC=N), 1375 (C-O), 536 (M-N), 448 (M-O)
(12)	15.0	Dia	28841	3377 (OH), 1608 (HC=N), 1377 (C-O), 528 (M-N), 451 (M-O)
(13)	14.6	4.45	8790, 17800, 29805	3470 (H ₂ O), 1620 (HC=N), 540 (M-N), 455 (M-O)

(14)	16.5	3.51	8696, 17871, 25719, 29778	3471 (H ₂ O), 1622 (HC=N), 544 (M-N), 459 (M-O)
(15)	15.4	1.70	8866, 17857, 29858	3470 (H ₂ O), 1623 (HC=N), 541 (M-N), 460 (M-O)
(16)	15.1	Dia	28932	3473 (H ₂ O), 1619 (HC=N), 543 (M-N), 463 (M-O)

¹H NMR Spectra

¹H NMR spectra of the ligands (**L**¹)-(**L**⁴) and their diamagnetic Zn(II) complexes were recorded in DMSO-d₆ and the details are provided in the experimental section. ¹H NMR spectra displayed³⁴ characteristic azomethine (-HC=N) protons at 8.53-8.65 ppm as a singlet providing a strong evidence for condensation of amino group of the ethanolamine with aldehydes. All of the ligands (**L**¹)-(**L**⁴) displayed aliphatic (-OH) proton at 5.63-5.99 ppm as a singlet and C₁₁-H and C₁₂-H protons at 4.50 and 5.85 ppm as triplet, respectively. The ligands (**L**¹)-(**L**³) possessed aromatic (-OH) proton at 9.88-9.93 ppm. Ligand (**L**¹) displayed other C_{3,5}-H and C₈-H protons as a double of doublet at 7.15-8.22 ppm, respectively but C₆-H and C₇-H protons appeared as a triplet at 7.41 and 7.53 ppm, respectively. Similarly, the ligand (**L**²) exhibited C₄-H and C₅-H protons at 7.0 and 7.45 ppm as triplet and, C₃-H and C₆-H protons as a doublet at 7.11 and 7.69 ppm respectively. The C₃-H and C₆-H protons of ligand (**L**³) were found at 7.12 and 8.10 ppm as a doublet and C₅-H proton observed at 7.50 ppm as a double of doublet. ¹H NMR spectra of the ligand (**L**⁴) showed the C₂-H, C₆-H and, C₃-H and C₅-H protons at 8.10 and 8.33 ppm as double of doublet. The disappearance of hydroxyl proton at 9.88-9.93 ppm in the spectra of Zn(II) complexes confirmed deprotonation and coordination of the hydroxyl-O with the metal atom. The coordination of the azomethine-N was evident by downfield shifting of all the proton signals in their Zn(II) complexes. A strong singlet was observed at 10.3 ppm in the Zn(II) complex (**16**) due to the coordination of water molecule with the Zn(II) metal atom. All protons underwent downfield shift by 0.05-0.12 ppm due to the increased conjugation on coordination with the zinc metal atom. The number of protons calculated from the integration curves³² and obtained values of the expected CHN analysis agreed well with each other.

¹³C NMR Spectra

The ¹³C-NMR spectra of the Schiff bases and their diamagnetic Zn(II) complexes were recorded in DMSO-d₆ and are reported along with their possible assignments in the experimental section and all the carbon atoms were found in the expected region. The ¹³C-NMR spectra of the Schiff base ligands (**L**¹)-(**L**⁴) displayed distinctive and representative (C₁₁, C₁₂) carbons of ethylene group and (C₁₃) carbons of azomethine (-HC=N) at 58.9-69.7 and 161.9-162.8 ppm respectively. The remaining other (C₁)-(C₁₀) carbons of aromatic rings were observed at 116.4-159.9 ppm. Downfield shifting of the azomethine carbons found in the uncomplexed Schiff bases from 161.9-162.8 ppm to 163.0-163.9 ppm in their Zn(II) complexes was due to shifting of electronic density towards the Zn(II) ion. Similarly, all carbons of methylene groups and aromatic rings being near to the coordination sites also showed downfield shifting by 0.5-1.1 ppm due to the increased conjugation and coordination with the metal atoms. The downfield shifting also confirmed the coordination of the azomethine to the zinc metal atom. Moreover, the presence of the number of carbons are well in agreement with the expected values³⁵. Furthermore, the conclusions drawn from these studies present further support to the modes of bonding discussed in their IR and ¹H NMR spectra.

Mass Spectra

The mass fragmentation pattern of the ligands (**L**¹)-(**L**³) followed the cleavage of C=N (exocyclic) and C=C bonds. The mass spectral data and the stable fragmentation values of the ligands have already been detailed in the experimental section. All the ligands showed pronounced molecular ion peaks. The data of the Schiff bases shown by mass spectra strongly confirmed the formation of the ligands possessing proposed structures and also, their bonding pattern.

Molar Conductances and Magnetic Measurements

Molar conductance studies of the metal(II) complexes (1)-(16) were carried out in DMF and their molar conductance data (14.6-16.9 ohm⁻¹ cm² mol⁻¹) showed that these complexes were non electrolytic³⁶ in nature. The magnetic moment (B.M) values of all the metal(II) complexes (**1**)-(**16**) were measured at room temperature. The observed magnetic moment value of Co(II)

complexes were found in the range of 4.35-4.53 B.M indicating that Co(II) complexes as a high-spin with potentially three unpaired electrons in an octahedral environment³⁷. The Ni(II) complexes displayed magnetic moment values in the range of 3.41-3.56 B.M indicative of two unpaired electrons per Ni(II) ion suggesting these complexes to have an octahedral³⁸ geometry. The measured magnetic moment values 1.66-1.74 B.M for Cu(II) complexes are indicative of one unpaired electron per Cu(II) ion for d^9 -system suggesting octahedral³⁹ geometry. All the Zn(II) complexes were found to be diamagnetic⁴⁰ as expected.

Electronic Spectra

The electronic spectra of Co(II) complexes generally showed⁴⁰ three absorption bands in the region 8650-8790, 17523-17800 and 29805-29841 cm^{-1} which may be assigned to $4T_{1g} \rightarrow 4T_{2g}(F)$, $4T_{1g} \rightarrow 4A_{2g}(F)$ and $4T_{1g} \rightarrow 4T_g(P)$ transitions respectively, and are suggestive of octahedral geometry around the Co(II) ion. The electronic spectral data of Ni(II) complexes showed⁴¹ the bands in the region 8635-8786, 17717-17871 and 25719-25717 cm^{-1} assigned respectively, to the d-d transitions of $3A_{2g}(F) \rightarrow 3T_{2g}(F)$ and $3A_{2g}(F) \rightarrow 3T_{1g}(F)$. Also a strong band due to metal to ligand charge transfer was appeared at 29738-29781 cm^{-1} . The electronic spectra of all the Cu(II) complexes exhibited⁴² absorption bands in the region at 8727-8937 and 17765-17892 cm^{-1} which may be assigned to the transitions $2E_g \rightarrow 2T_{2g}$. The high energy band at 29788-29858 cm^{-1} was due to forbidden ligand to metal charge transfer. On the basis of electronic spectra, octahedral geometry around the Cu(II) ion was suggested. The Zn(II) complexes did not show any d-d transition thus showing diamagnetic nature and their spectra were dominated only by a charge transfer band⁴³ at 28841-28932 cm^{-1} .

Biological Screening

Antibacterial Bioassay (*in vitro*)

The newly produced Schiff bases (**L¹**)-(**L⁴**) and their metal(II) complexes (**1**)-(**16**) were screened of their *in-vitro* antibacterial activity against *Escherichia coli*, *Shigella flexneri*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Staphylococcus aureus* and *Bacillus subtilis* bacterial strains according to the standard procedures²⁴ and results are reported in **Table 3**. The obtained results were compared with those of the standardized drug sample of imipenem. The synthesized ligand

(**L**¹) displayed a weaker (07-08 mm clearance zone (cz) or zone of inhibition) activity against *Escherichia coli* and *Bacillus subtilis* and the remaining strains displayed moderate (10-13 mm) activity. Ligand (**L**²) presented a weaker (8 mm) activity against *Salmonella typhi* and the remaining strains showed moderate (9-13 mm) activity. Ligand (**L**³) demonstrated moderate (11-12 mm) activity against *Shigella flexneri*, *Pseudomonas aeruginosa* and *Bacillus subtilis* and, other remaining strains observed significant (16-17 mm) activity. The ligand (**L**⁴) experienced overall significant (15-17 mm) activity. The metal complex (**1**) showed moderate (14 mm) activity against *Escherichia coli* and *Bacillus subtilis* and other remaining strains experienced significant (15-19 mm) activity. Complex (**2**) showed moderate (12-14 mm) activity against *Pseudomonas aeruginosa* and *Bacillus subtilis* and left behind strains practiced significant (17-18 mm) activity. Compound (**3**) exhibited moderate (12-13 mm) activity against *Salmonella typhi* and *Bacillus subtilis* and, left over demonstrated significant (16-18 mm) activity. Beside this, the compound (**4**) revealed significant (15-20 mm) activity against all bacterial strains except *Escherichia coli* which observed moderate (13 mm) activity. Also, the complexes (**5**) and (**6**) displayed moderate (12-14 mm) activity against *Salmonella typhi* and *Staphylococcus aureus* and, remaining strains revealed significant (17-19 mm) activity. However, the complexes (**7**)-(**16**) displayed overall significant (15-25 mm) activity against all bacterial strains. The data reported in **Table 3** clearly indicates that (**L**⁴) exhibited overall good bacterial activity as compared to other three ligands. The Zn(II) complex (**16**) of (**L**⁴) were found to be the most active complexes. The metal(II) complexes showed⁴¹ higher activity results upon complexation rather than their uncomplexed Schiff bases.

Table 3. Antibacterial Bioassay of Ligands (**L**¹)-(**L**⁴) and Metal(II) Complexes (**1**)-(**16**)

[Zone of Inhibition (mm)]								
Compounds	Gram-negative				Gram-positive			
	(a)	(b)	(c)	(d)	(e)	(f)	(SA)	Average
(L ¹)	08	13	11	10	13	07	2.50	10.33
(L ²)	13	11	12	08	09	11	1.86	10.67
(L ³)	16	12	11	17	16	12	2.61	14.00
(L ⁴)	16	17	15	17	16	15	0.89	16.00

(1)	14	19	17	15	19	14	2.59	16.50
(2)	17	18	12	17	18	14	2.45	16.00
(3)	16	17	18	13	16	12	2.34	15.33
(4)	13	16	19	16	20	15	2.59	16.50
(5)	18	17	19	14	12	18	2.73	16.33
(6)	16	18	16	13	14	16	1.76	15.50
(7)	17	19	15	16	16	16	1.38	16.50
(8)	20	17	19	15	16	17	2.50	17.67
(9)	20	21	17	22	22	18	2.10	20.00
(10)	22	16	19	19	23	21	2.53	20.00
(11)	20	17	16	21	19	20	1.94	18.83
(12)	18	24	19	23	20	21	2.32	20.83
(13)	21	23	16	20	19	18	2.58	19.67
(14)	20	17	21	22	24	22	2.37	21.00
(15)	19	22	17	19	25	20	2.80	20.33
(16)	22	21	22	24	21	21	1.17	21.83
SD	25	26	25	27	27	28	1.17	25.83

Average Activity of Ligand (**L¹**)-(L⁴) = 12.75 mm; Average Activity of Complexes **(1)**-(**16**) = 18.74 mm; **(a)** *E. Coli* **(b)** *S. flexneri* **(c)** *P. Aeruginosa* **(d)** *S. Typhi* **(e)** *S. Aureus* **(f)** *B. Subtilis*; **SD**: Standard Drug (Imipenem); weaker = 0-08 mm, moderate = 09-14 mm, above 14 mm = significant, **SA** = Statistical Analysis

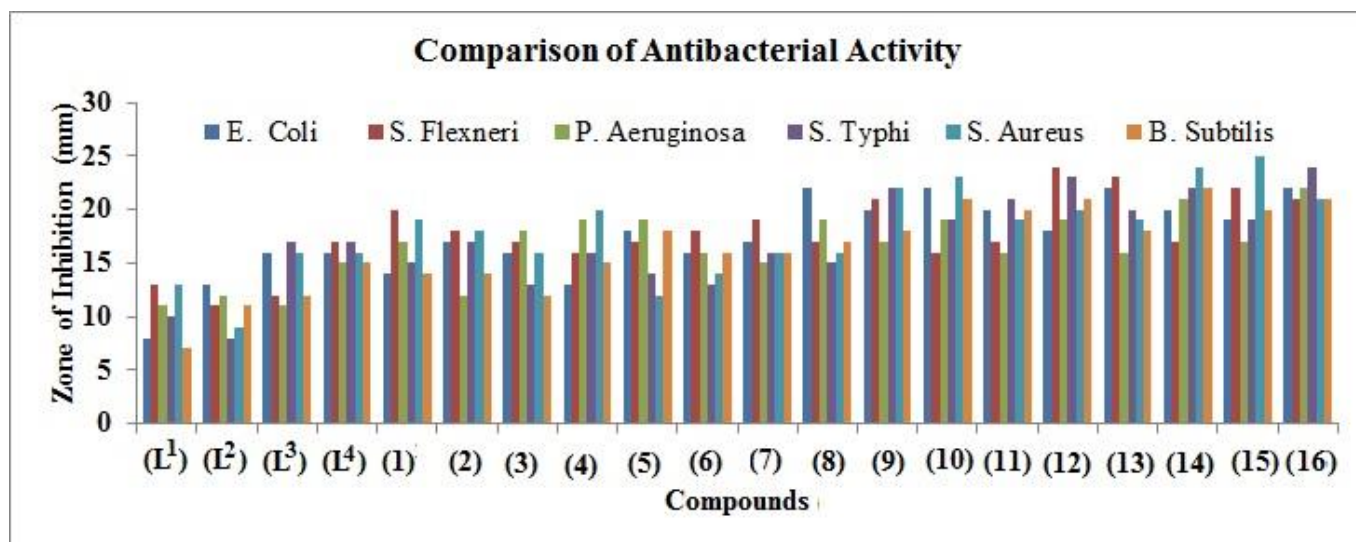


Figure 1. Comparison of Antibacterial Activity of Schiff bases versus Metal(II) Complexes

Antifungal Bioassay (*in-vitro*)

The antifungal screening of all the synthesized compounds was carried out against *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glabrata* fungal strains **Table 4** according to the literature protocol²². The results of inhibition were compared with the results of standard drugs, miconazole and amphotericin B. Ligand (**L¹**) exhibited significant (55%) activity against *Aspergillus flavus* fungal strain, moderate (37-45%) activity against *Trichophyton longifusus*, *Microscopum canis* and *Candida glabrata* and weaker (17%) activity against *Candida albicans* and but inactive against *Fusarium solani* begging further investigation why that may be? Similarly, the ligand (**L²**) possessed significant (56%) activity against *Candida albicans* and moderate (38-49%) activity against *Trichophyton longifusus*, *Aspergillus flavus*, *Fusarium solani*, weaker (30%) activity against *Candida glabrata* but no activity was observed in *Aspergillus flavus*. However, (**L³**) and (**L⁴**) displayed overall significant (55-63%) activity against all fungal strains. The complex (**1**) displayed significant (61-63%) activity against *Trichophyton longifusus*, *Aspergillus flavus* and *Candida glabrata* fungal strains, moderate (37-50%) activity against *Candida albicans* and *Microsporum canis*, and weaker (16%) activity against *Fusarium solani*. Likewise, complex (**2**) had significant (55-77%) activity against *Trichophyton longifusus*, *Aspergillus flavus*, *Microsporum canis*, and *Candida glabrata*, and displayed weaker (25-26%) activity against

remaining two strains. Similarly the compound **(3)** demonstrated significant (55-69%) activity against *Trichophyton longifusus*, *Aspergillus flavus*, *Microsporum canis*, and *Candida glabrata*, moderate (42%) against *Candida albicans* and weaker (23%) activity against *Fusarium solani*. The complex **(4)** comparably possessed significant (55-65%) activity against *Trichophyton longifusus*, *Aspergillus flavus*, *Microsporum canis*, and *Candida glabrata* and moderate (36-37%) activity was observed with rest of the fungal strains. On the other hand, the compound **(5)**-**(8)** showed overall significant (55-75%) activity against all strains except *Microsporum canis* which displayed weaker (17-30%) activity. The compounds **(9)**-**(16)** displayed overall significant (55-78%) activity against fungal strains due to Br and NO₂ groups attached with the aromatic rings. **(L⁴)** showed overall good fungal activity as compared to other three ligands due to nitro substitution. The Co(II) complex **(14)** of **(L⁴)** was found to be the most active complex. The metal(II) complexes showed enhanced⁴⁵ activity results rather than their uncomplexed Schiff bases upon complexation.

Table 4. Antifungal Bioassay of Ligands **(L¹)**-**(L⁴)** and Metal(II) Complexes **(1)**-**(16)**

Compounds	[% Inhibition (mm)]							Average
	(a)	(b)	(c)	(d)	(e)	(f)	(SA)	
(L¹)	45	17	55	37	00	40	20.18	32.33
(L²)	38	56	49	00	43	30	19.77	36.00
(L³)	56	60	61	56	63	59	2.79	59.17
(L⁴)	62	58	59	63	61	55	2.94	59.67
(1)	62	37	63	49	16	61	18.63	48.00
(2)	55	25	75	77	26	58	22.81	52.67
(3)	59	42	62	55	23	69	16.66	51.67
(4)	65	36	64	56	37	57	12.91	52.50
(5)	57	68	66	17	75	66	20.97	58.17
(6)	61	69	72	28	69	71	16.94	61.67

(7)	55	73	67	30	66	75	16.72	61.00
(8)	56	64	68	25	68	69	17.03	58.33
(9)	71	75	70	67	72	74	2.88	71.50
(10)	75	69	57	73	70	67	6.32	68.50
(11)	69	74	70	65	69	65	3.39	68.67
(12)	70	78	68	74	73	60	6.19	70.50
(13)	72	75	70	61	72	64	5.37	69.00
(14)	78	65	57	73	70	67	7.20	68.33
(15)	69	58	70	65	72	65	5.01	66.50
(16)	75	68	72	77	79	68	4.62	73.17
SD	A	B	C	D	E	F	-	-

Average Activity of Ligands (**L¹**)-(L⁴) = 46.79%; Average Activity of Complexes (**1**)-(16) = 62.51%; (**a**) *T. Longifusus* (**b**) = *C. Albicans* (**c**) = *A. Flavus* (**d**) = *M. Canis* (**e**) = *F. Solani* (**f**) = *C. Glabrata* SD = Standard Drugs MIC $\mu\text{g/mL}$; A = Miconazole (70 $\mu\text{g/mL}$: 1.6822×10^{-7} M/mL), B = Miconazole (110.8 $\mu\text{g/mL}$: 2.6626×10^{-7} M/mL), C = Amphotericin B (20 $\mu\text{g/mL}$: 2.1642×10^{-8} M/mL), D = Miconazole (98.4 $\mu\text{g/mL}$: 2.3647×10^{-7} M/mL), E = Miconazole (73.25 $\mu\text{g/mL}$: 1.7603×10^{-7} M/mL), F = Miconazole (110.8 $\mu\text{g/mL}$: 2.6626×10^{-7} M/mL); weaker = 0-33%, moderate = 34-54%, 55-100% = significant; SA = Statistical Analysis.

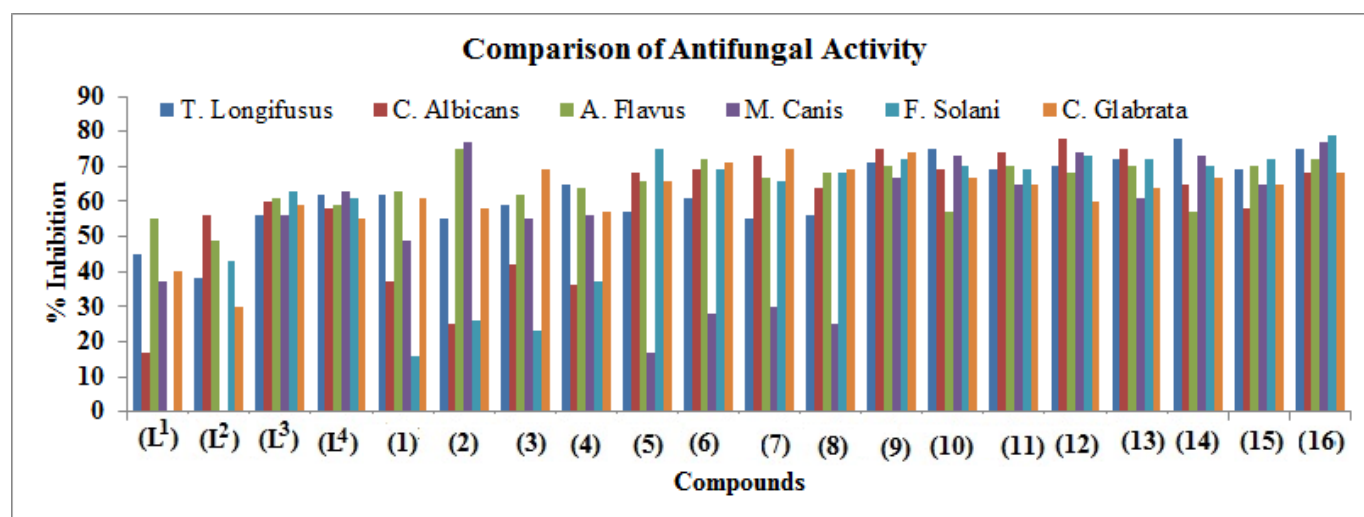


Figure 2. Comparison of Antifungal Activity of Schiff bases versus Metal(II) Complexes

Minimum Inhibitory Concentration (MIC)

The synthesized ligands and their transition metal(II) complexes showing promising antibacterial activity (> 80%) were selected for MIC studies i.e. (9), (10) and (12)-(16) and the results are reported in **Table 5**. The MIC values of these compounds fall in the range 23.11 to 46.62g/mL. Amongst these, the compound (14) was found to be the most active possessing maximum inhibition 16.11 µg/mL against bacterial strain *S. Aureus*.

Cytotoxicity (In-vitro)

The Schiff bases and their vanadyl(IV) complexes were screened for their cytotoxicity (brine shrimp bioassay) by using Meyer protocol²⁶. The data recorded in **Table 6** indicate that none of the compounds either ligands or complexes showed cytotoxicity (1.64×10^{-3} to 4.71×10^{-3}) against *Artemia salina*. This activity relationship may help to serve as a basis for future direction towards the development of certain cytotoxic agents for clinical applications.

Table 5. Minimum Inhibitory Concentration (µg/mL) of the Selected Compounds (9), (10) and (12)-(16) against Selected Bacteria.

Compounds	<i>E. Coli</i>	<i>S. Flexneri</i>	<i>P. Aeruginosa</i>	<i>S. Typhi</i>	<i>S. Aureus</i>
(9)	-	46.21	-	37.16	25.17
(10)	30.16	-	-	-	39.24
(12)	-	36.35	-	43.22	-
(13)	23.71	28.67	-	-	-
(14)	-	-	32.11	46.62	16.11
(15)	-	25.00	-	-	26.35
(16)	39.10	18.17	42.65	25.31	-

Table 6. Cytotoxicity (*In vitro*) of Ligands (L¹)-(L⁴) and their Metal(II) Complexes (1)-(16)

Compounds	LD ₅₀ (M/mL)	Compounds	LD ₅₀ (M/mL)	Compounds	LD ₅₀ (M/mL)
(L ¹)	$>2.19 \times 10^{-3}$	(4)	$>1.64 \times 10^{-3}$	(11)	$>4.71 \times 10^{-3}$
(L ²)	$>1.81 \times 10^{-3}$	(5)	$>3.19 \times 10^{-3}$	(12)	$>2.68 \times 10^{-3}$
(L ³)	$>3.11 \times 10^{-3}$	(6)	$>4.04 \times 10^{-3}$	(13)	$>2.51 \times 10^{-3}$
(L ⁴)	$>2.19 \times 10^{-3}$	(7)	$>4.59 \times 10^{-4}$	(14)	$>2.11 \times 10^{-3}$

(1)	$>3.81 \times 10^{-3}$	(8)	$>2.81 \times 10^{-3}$	(15)	$>4.19 \times 10^{-4}$
(2)	$>2.11 \times 10^{-3}$	(9)	$>3.15 \times 10^{-3}$	(16)	$>3.81 \times 10^{-3}$
(3)	$>4.10 \times 10^{-3}$	(10)	$>1.98 \times 10^{-3}$		

Conclusions

The synthesized ethanol derived Schiff bases act as bi and tridentate ligands for coordination with the Co(II), Cu(II), Ni(II) and Zn(II) metal atoms. Physical (magnetic and molar conductance), spectral (IR, NMR, electronic) and analytical (C, H, N and V percentage) data confirmed that the Schiff base ligands are coordinated with the Co(II), Cu(II), Ni(II) and Zn(II) metal atoms via azomethine-N, naphthalene-O, salicylidene-O and ethanol-O showing an octahedral geometry. The obtained results of antibacterial and antifungal activities indicated that the metal complexes possessed better biological activity against one or more bacterial and/or fungal strains as compared to their parent uncomplexed ligands. It can be asserted that azomethine-N, nitro, bromo and oxygen were the functional groups in the compounds potentially responsible for the enhancement of bacterial and fungal activities. However, brine shrimp assays revealed that these compounds were limited in their cytotoxicity hinting at some divergent apoptotic mechanisms.

Conflict of Interests

The authors declare no conflict of interest.

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